



CURRICULUM VITAE

LELAND SHAPIRO MD, FACP

PERSONAL INFORMATION

Date of Birth: June 26, 1958

Place of Birth: Memphis, Tennessee

Home Address and Telephone: 9123 East Mississippi Avenue, Apt. 1303, Denver, CO, 80231. Tel (303) 337-5108.

Professional Address and Telephone: University of Colorado Health Sciences Center Division of Infectious Diseases, Department of Medicine, 4200 East Ninth Ave., Box B168, Denver, CO 80262. Tel (303) 315-3558.

Denver Veteran's Affairs Medical Center
1055 Clermont St. (111L)
Denver, CO 80220

Social Security Number: 020-46-6026.

PRESENT ACADEMIC RANK AND POSITION

Assistant Professor of Medicine, University of Colorado School of Medicine.

Board Certification:

1989- certified by the American Board of Internal Medicine as specialist in Internal Medicine

1992- certified by the American Board of Internal Medicine as sub-specialist in Infectious Diseases.

EDUCATION

College/University:

1976-1980 Tufts University, College of Liberal Arts, Medford, MA

•B.A. with double major in philosophy and psychology. Dean's List.

•*Magna cum Laude* in both Philosophy and Psychology.

3/22/97

Graduate School:

1980-1981 Tufts University, Graduate School of Arts and Sciences.
•Graduate Fellow in Philosophy.
•Teaching Assistantships in courses on "Logic" and "Theories of Human Nature".

Medical School:

1981-1986 University of Massachusetts School of Medicine, Worcester, MA.
•M.D. - June 1986.

1983-1984 Pre-Doctoral Fellow in Pathology, Department of Pathology, University of Massachusetts School of Medicine, Worcester, MA.
•Performed functions of junior resident in Pathology, including frequent presentations to house staff; cut, described, and made microscopic diagnoses in over 3,000 surgical specimens; personally conducted 40 autopsies.

Internship/Residency:

1986-1989 University of North Carolina Hospital, Chapel Hill, NC
•Internship and Residency in Internal Medicine.

Chief Residency:

1989-1990 Moses H Cone Memorial Hospital, Greensboro, NC
•Chief Medical Resident.

Fellowship:

1990-1995 New England Medical Center. Division of Internal Medicine, Department of Geographic Medicine and Infectious Diseases. Trained in the laboratory of Dr. Charles A. Dinarello.
•Clinical-Research Fellowship.

HONORS/AWARDS

1997 Clinical teaching award, Division of Infectious Diseases, University of Colorado Health Sciences Center.

1997 Editorial Board member, Scientific Review of Alternative Medicine.

1996 Recipient of the first prize, Outstanding Young Investigator Award for original research at the Meeting of the International Cytokine Society (10/96).

1994 Recipient of the Maxwell Finland award as outstanding young research investigator in the Infectious Diseases Division of the New England Medical Center.

1989-1990 Recipient of the Joseph B. Stephens memorial award for outstanding clinical instructor at Moses H Cone Memorial Hospital, Greensboro, NC.

1988-1989 Awarded Ciba-Geigy prize for outstanding academic medical resident at North Carolina Memorial Hospital, Chapel Hill, NC.

PREVIOUS PROFESSIONAL POSITIONS AND APPOINTMENTS

See above.

EDUCATION/TEACHING

Medical School:

1983 Guest Lecturer, Worcester Medical Society's Forum for the Study of Values, MA.
•Topic; "The Impact of John Rawls' *A Theory of Justice* on medical ethics".

1983-1984 Pre-Doctoral Fellow in Pathology, Department of Pathology, University of Massachusetts School of Medicine, Worcester, MA.
•Numerous case and teaching presentations to hospital staff and students.
Frequent divisional conference presentations

Graduate School:

1980-1981 Tufts University, Graduate School of Arts and Sciences.
•Graduate Fellow in Philosophy.
•Teaching Assistantships in courses on "Logic" and "Theories of Human Nature" (one semester each).

Other:

1996 Attending Physician, University of Colorado School of Medicine
•Infectious Diseases subspecialty service.
•General Internal Medicine service.
(both at the University of Colorado Health Sciences Center, one month each).

1989-1990 Attending Physician, Moses H Cone Memorial Hospital,
Greensboro, NC

•Chief Medical Resident. Attended on the teaching services of Internal Medicine
and the outpatient clinic for 10 months.

**INSTITUTIONAL, DEPARTMENTAL, AND DIVISIONAL ADMINISTRATIVE
RESPONSIBILITIES, COMMITTEE MEMBERSHIPS, AND OTHER ACTIVITIES**

1989-1990 Peer-Review Committee, Moses H Cone Memorial
Hospital Hospital, Greensboro, NC.

PROFESSIONAL AND SOCIETY MEMBERSHIPS

- Fellow - American College of Physicians (5/98).
- American Medical Association.
- Massachusetts Medical Society.
- Member International Cytokine Society (10/93-present)
- Member Infectious Diseases Society of America (5/96)
- Member, New York Academy of Sciences 4/97

RESEARCH INTERESTS

•Our current primary focus is on the role of the endogenous serine protease/alpha-1 antitrypsin (AAT) system in HIV pathogenesis. We have expanded these studies to include investigations of serine proteases and AAT in the pathogenesis of other microbiological pathogens; we also study the role of serine proteases/AAT in inflammation. Our second major focus involves the recently described cytokine Interleukin-18. We investigate the role of IL-18 in HIV pathogenesis in several *in vitro* models. Other projects include development of protein assays using electrochemiluminescence. Collaborative investigations include measurement of cytokines in patients with various diseases. We have recently completed a phase 1-2 study of Interleukin-10 administration to HIV-infected patients.

PUBLICATIONS

Original Publications in Peer Reviewed Journals

Shapiro L, Clark BD, Orencole SF, Poutsakia DD, Granowitz EV, Dinarello CA. Detection of tumor necrosis factor soluble receptor p55 in blood samples from healthy and endotoxemic humans. *J Infect Dis*, 167:1344-1350, 1993.

Shapiro L, Zhang X, Rupp RG, Wolff SM, Dinarello CA. Ciliary neurotrophic factor is an endogenous pyrogen. *Proc Natl Acad Sci USA*, 90:8614-8618, 1993.

Granowitz EV, Porat R, Mier JW, Orencole SF, Callahan MV, Cannon JG, Lynch EA, Ye K, Poutsakia DD, Vannier EV, Shapiro L, Pribble JP, Stiles DM, Catalano MA, Wolff SM, Dinarello CA. Hematologic and immunologic effects of an interleukin-1 receptor antagonist coinfusion during low-dose endotoxemia in healthy humans. *Blood*, 82:2985-2990, 1993.

Tilg H, Shapiro L, Atkins MB, Dinarello CA, Mier JW. Induction of circulating and erythrocyte-bound IL-8 by IL-2 immunotherapy and suppression of its in vitro production by IL-1 receptor antagonist and soluble tumor necrosis factor receptor (p75) chimera. *J Immunol*, 151:3299-3307, 1993.

Tilg H, Pape D, Trehu E, Shapiro L, Atkins MB, Dinarello CA, Mier JW. A method for the detection of erythrocyte-bound interleukin-8 in humans during interleukin-1 immunotherapy. *J Immunol Methods*, 163:253-258, 1993.

Santos AA, Shapiro L, Lynch EA, Brown EF, Chambers E, Jacobs DO, Dinarello CA, Mannick J, Wilmore DW. Tumor necrosis factor soluble receptor p55: endogenous counter-regulatory glycoprotein. *Surgical Forum*, 44:119-121, 1993.

Tilg H, Vogel W, Wiedermann CJ, Shapiro L, Herold M, Judmaier G, Dinarello CA. Circulating interleukin-1 and tumor necrosis factor antagonists in liver diseases. *Hepatology*, 18 (5):1132-1138, 1993.

Shapiro L, Panayotatos N, Meydani SN, Wu D, Dinarello CA. Ciliary neurotrophic factor combined with soluble receptor inhibits synthesis of proinflammatory cytokines and prostaglandin-E₂ *in vitro*. *Exp Cell Res*, 215:51-56, 1994.

Pereira BJJ, Shapiro L, King AJ, Falagas ME, Strom JA, Dinarello CA. Plasma levels of IL-1 β , TNF α and their specific inhibitors in undialyzed chronic renal failure, CAPD, and hemodialysis patients. *Kidney International*, 45:890-896, 1994.

Kaplanski G, Farnarier C, Kaplanski S, Porat R, Shapiro L, Bongrand P, Dinarello CA. Interleukin-1 induces interleukin-8 secretion from endothelial cells by a juxtracrine mechanism. *Blood*, 84:4242-4248, 1994.

Mandrup-Poulsen T, Pociot F, Molvig J, Shapiro L, Nilsson P, Emdal T, Roder M, Kjems LL, Dinarello CA, Nerup J. Monokine antagonism is reduced in patients with insulin-dependent diabetes mellitus. *Diabetes*, 43 (10):1242-1247, 1994.

Tilg H, Trehu E, Shapiro L, Pape D, Atkins MB, Dinarello CA, Mier JW. Induction of circulating soluble tumor necrosis factor receptor and interleukin-1 receptor antagonist following interleukin-1 α infusion in humans. *Cytokine*, 6:215-219, 1994.

Latini R, Bianchi M, Correale E, Dinarello CA, Fantuzzi G, Fresco C, Maggioni AP, Mengozzi M, Romano S, Shapiro L, Sironi M, Tognoni G, Turato R, Ghezzi P. Cytokines in acute myocardial infarction: selective increase of circulating tumor necrosis factor, its soluble receptor and interleukin-1 receptor antagonist. *J Cardiovasc Pharm*, 23:1-6, 1994

Fantuzzi G, Benigni F, Sironi M, Conni M, Carelli M, Cantoni L, Shapiro L, Dinarello CA, Sipe JD, Ghezzi, P. Ciliary neurotrophic factor (CNTF) induces serum amyloid A, hypoglycemia and anorexia, and potentiates IL-1 induced corticosterone and IL-6 production in mice. *Cytokine*, 7 (2):150-156, 1995.

Chernoff AE, Granowitz EV, Shapiro L, Vannier E, Lonnemann G, Angel JB, Kennedy JS, Rabson AR, Wolff SM, Dinarello, CA. A randomized, controlled trial of IL-10 in humans. Inhibition of inflammatory cytokine production and immune response. *J Immunol*, 95:5492-5499, 1995.

Lonnemann G, Shapiro L, Engler-Blum G, Muller GA, Koch KM, Dinarello CA. Cytokines in human renal interstitial fibrosis. I. Interleukin-1 is a paracrine growth factor for cultured fibrosis-derived kidney fibroblasts. *Kidney International*, 47:837-844, 1995.

Shapiro L, Dinarello, CA. Osmotic regulation of cytokine synthesis *in vitro*. *Proc Natl Acad Sci USA*, 92:12230-12234, 1995.

Fuchs AE, Granowitz EV, Shapiro L, Vannier E, Lonnemann G, Angel JB, Kennedy JS, Rabson AR, Radwanski E, Cutler DL, Grint P, Dinarello CA. Clinical, hematologic, and immunologic effects of interleukin-10 in humans. *J Clin Immunol*, 16:291-303, 1996

Trehu EG, Mier JW, Dubois JS, Sorce D, Klempner MS, Epstein M, Dinarello CA, Shapiro L, Kappler K, Ronayne L, Atkins MB. Phase 1 trial of interleukin 2 in combination with the soluble tumor necrosis factor receptor p75 IgG chimera. *Clin Cancer Res*, 2:1341-1351, 1996.

DuBois J,S Trehu EG, Mier JW, Shapiro L, Epstein M, Klempner MS, Dinarello d, Kappler K, Ronayne L, Rand W, Atkins MB. Randomized placebo-controlled clinical trial of high-Dose interleukin-2 in combination with a soluble p75 tumor necrosis factor receptor immunoglobulin G chimera in patients with advanced melanoma and renal cell carcinoma. *J Clin Oncol*, 15: 1052-1062, 1997.

Shapiro, L, Dinarello, C.A. Hyperosmotic stress as a stimulant for proinflammatory cytokine production. *Exp Cell Res*, 231:354-362, 1997.

Shapiro L, Heidenreich KA., Meintzer M-K, Dinarello CA. Role of p38 mitogen activated protein kinase in human immunodeficiency virus type 1 production *in vitro*. *Proc Natl Acad Sci USA*, 95:7422-7426, 1998.

Shapiro L, Puren AJ, Barton HA, Novick D, Peskind RL, Shenkar R, Gu Y, Su MS-S, Dinarello CA. Interleukin-18 stimulates human immunodeficiency virus type-1 in monocytic cells. *Proc Natl Acad Sci USA*, 95: 12550-12888, 1998.

Larsen CM, Wadt KAW, Juhl LF, Anderson HU, Karlson AE, Su MS-S, Seedorf K, Shapiro L, Dinarello CA, Mandrup-Poulsen T. Interleukin-1 β -induced rat pancreatic islet nitric oxide synthesis requires both the p38 and extracellular signal-regulated kinase 1/2 mitogen activated protein kinases. *J Biol Chem*, 273:15294-15300, 1998.

Reznikov LL, Puren AJ, Fantuzzi G, Muhl H, Shapiro L, Yoon D-Y, Cutler DL, Dinarello CA. Spontaneous and inducible cytokine responses in healthy humans receiving a single dose of IFN- α 2b: increased production of interleukin-1 receptor antagonist and suppression of IL-1-induced IL-8. *J Interferon and Cytokine Res*, 18:897-903, 1998.

Angel JB, Jacobson MA, Skolnik PR, Giordano M, Shapiro L, LeBeat A, Greaves W, Fuchs AC. A multicenter, randomized, double-blind, placebo-controlled trial of recombinant human interleukin-10 in HIV-infected subjects. *AIDS*, 14:2503-2508, 2000.

Shapiro L, Pott GB, Ralston AH. Alpha-1-antitrypsin inhibits human immunodeficiency virus type 1. *FASEB Journal*, 15:115-122, 2001.

Chan E, Ralston AH, Shapiro L. Does reduced alpha-1-antitrypsin activity account for the link between cigarette smoking and idiopathic pulmonary fibrosis? Chest, 129:72S-74S, 2001.

Choi H-J, Dinarello CA, Shapiro L. Interleukin-18 inhibits human immunodeficiency virus type 1 production in peripheral blood mononuclear cells. J Infect Dis, 184: 560-568, 2001.

Choi H-J, Dinarello CA, Shapiro L. Reply to the editor; Interleukin-18 inhibits human immunodeficiency virus type 1 production in peripheral blood mononuclear cells. J Infect Dis, 185: 998-999, 2002.

Reviews and Book Chapters

Shapiro L, Gelfand JA. Cytokines and sepsis, pathophysiology and therapy. New Horizons 1:13-22, 1993.

Shapiro L, Gelfand JA. Cytokines in disease. Textbook of Critical Care Medicine, 3rd Edition, Grenvik A, Holbrook PR, Shoemaker, WC, (Editors) WB Saunders Company, Philadelphia. 1999, 578-586.

Chernoff AE, Granowitz EV, Shapiro L, Vannier E, Lonnemann G, Angel JB, Orencole SF, Kennedy JS, Zhang X-X, Wen H-D, Donaldson EC, Radwanski E, Cutler DL, Wolff SM, and Dinarello CA. A Phase I Study of Intertleukin-10 in Healthy Humans: Safety and Effects on Cytokine Production. Interleukin-10. deVries, JE, and de Waal Malefyt, R (Editors) R./G. Landes Company, 1995, 95, 592-5499.